Hypothyroidism and Non-Alcoholic Fatty Liver Disease: Association and Effect of Levothyroxine Replacement Therapy

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Abstract:

Background: The association between hypothyroidism and non-alcoholic fatty liver disease (NAFLD) is increasingly studied with controversial results, and evidence regarding the effect of levothyroxine replacement therapy on NAFLD are lacking. Objectives: to examine the association between overt hypothyroidism and NAFLD, and to test the effect of levothyroxine (LT4) replacement therapy on NAFLD among subjects with overt hypothyroidism. Methods: 325 recently diagnosed overt hypothyroidism subjects were compared to 325 age, sex, and BMI matched subjects regarding metabolic characteristics, serum liver enzymes, and ultrasound diagnosed NAFLD. The same comparison was performed on subjects with NAFLD in the case group before and after 12 months of LT4 replacement therapy. Results: The mean age of participants was 45.22±5.04 years old, and 369 (56.8) were females. Subjects with overt hypothyroidism had a significantly higher prevalence of NAFLD [146 (44.9) versus 83 (25.5), p < 0.001], and higher means of metabolic variables, liver enzymes, and ultrasound liver measurements (p < 0.5). At 12 months of LT4 therapy, there was 35.6% reduction in the prevalence of NAFLD (p< 0.001), and significantly reduced values of metabolic variables, and serum liver enzymes (p < 0.05) among subjects with NAFLD in the case group. Conclusions: Overt hypothyroidism was significantly associated with NAFLD. Moreover, 12 months LT4 replacement therapy significantly reduced the prevalence of NAFLD.

Keywords: Levothyroxine Replacement, Non-alcoholic Fatty Liver Disease, Overt Hypothyroidism

Introduction:

When the liver becomes a site for fat accumulation, a cascade of clinical consequences will arise, collectively are referred to as non-alcoholic fatty liver disease (NAFLD).¹ Its clinical entities ranges from fatty liver disease to non-alcoholic steatohepatitis (NASH), where persistent inflammation may proceed to liver cirrhosis with the consequence of a greater risk of hepatocellular carcinoma, and increased demand for liver transplantation.²

NAFLD is considered the commonest chronic liver disease, with a world-wide prevalence estimated at 20% to 30%.³ Its prevalence is rapidly increasing e.g. the prevalence in the United States has been increasing from 18% in 1988-1991, to 31% in 2017.⁴

The rapidly increasing prevalence of NAFLD is parallel to the universal upsurge in the prevalence of the features of metabolic syndrome; central adiposity, hyperlipidemia, glucose intolerance/diabetes type 2, and arterial hypertension.⁵ Primary NAFLD may precede, coexist, or follow metabolic syndrome, however, several factors have been identified to produce secondary NAFLD including viral infections, steatogenic drugs and alcohol consumption.⁶

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NAFLD secondary to thyroid diseases; subclinical and overt hypothyroidism, has been recently the focus of much research based on the fact that thyroid hormones are significantly incorporated in the regulation of body fat distribution, energy expenditure, and carbohydrate and lipid metabolism.\(^{(7)}\) Additionally, it is widely accepted that conditions causing disturbed serum concentrations of thyroid hormones may predispose to metabolic syndrome, \(^{(5)}\) thus correlation to NAFLD.\(^{(8)}\)

While the global burden of NAFLD is elucidated, there is no specific pharmacologic treatment, and therapies to improve NAFLD still investigational. \(^{(9)}\) The increasing evidence of the association between hypothyroidism and NAFLD has urged scientists to consider hypothyroidism-induced NAFLD as a distinct disease entity with a likely favorable effect on NAFLD on normalizing thyroid hormones.\(^{(10)}\)

Levothyroxine (LT4) is the standard replacement therapy for hypothyroidism and is associated, through metabolic correction, with a substantial reduction of body weight and serum lipids,\(^{(11)}\) therefore, appropriate LT4 supplementation, to treat hypothyroidism, yield benefits on NAFLD was suggested. \(^{(12)}\) Apparently, few studies have examined the effect of LT4 replacement, on the course of treatment of hypothyroidism, on the prevalence of NAFLD and liver profile.\(^{(12, 13)}\) It is though that the increasingly prevalent and troublesome liver disease; NAFLD, is commonly disregarded by endocrinologists. Likewise, hematologists seem to disregard the underlying hypothyroidism in individuals presented with NAFLD. Therefore, the objectives of the present study were to assess the association between hypothyroidism and NAFLD to alert the practicing physicians for the consequences of hypothyroidism on the liver. Moreover, this study was purposed to examine the effect of LT4 on NAFLD, aiming to offer an alternative pharmacologic treatment of NAFLD.

**Methods:**

This case control study and quasi experimental trial was conducted during the period from February 2017 to December 2019, and involved subjects attended the internal medicine and family medicine clinics of Umm Al-Qura University Medical Center, Makkah, Saudi Arabia.

**Inclusion criteria:** Subjects of both sexes, and between the ages 18 to 65 years old.

**Exclusion criteria:** (1) Subjects with known liver disease including viral hepatitis, (2) history of current or past alcohol consumption of any amount, (3) use of hepatotoxic medicines or herbal remedies, and (4) other diseases incorporated in fatty liver disease.\(^{(14)}\)

Participants were divided into two groups: (1) **Case group:** included subjects with recently diagnosed overt hypothyroidism confirmed with high thyroid stimulating hormone (TSH) above 4.2 mIU/mL, and low free thyroxin (FT4) below
and are not on levothyroxine replacement therapy yet; (2) **Control group:** included subjects age, sex, and BMI matched with the case group, and without thyroid dysfunction confirmed with normal serum levels of TSH, FT4, and free tri-iodothyronine (FT3).

**Baseline Variables:** Participants’ full history including socio-demographics, medical, and medications history was gathered using standardized interview, and findings were documented. Body weight, height and waist circumference were measured. Body mass index (BMI) was calculated by dividing weight by the square of the height. Blood pressure was measured after 10-min seated rest, with cuff-size suitable for participant’s arm circumference. The average of three consecutive measurements was obtained to determine the systolic and diastolic blood pressure.

**Laboratory investigations:** Average of 25 ml of venous blood was obtained from each participant after 10 hours of overnight fasting. Total cholesterol (TC), triglycerides (TG), low density lipoprotein cholesterol (LDL-C), high density lipoprotein cholesterol (HDL-C), fasting blood glucose (FBG), and liver enzymes including alanine aminotransferase (ALT), aspartate aminotransferase (AST), γ-glutamyl transferase (GGT), alkaline phosphatase (ALP), and total bilirubin were measured using the Beckman LX-20 auto-analyzer (Beckman Coulter, La Brea, CA, USA). Thyroid hormones including TSH, FT4, and FT3 were measured using an Elecsys® 2010 Disk & Rack Analyzers (Roche Diagnostics, 9115 Hague Road, Indianapolis, USA). All measurements were performed according to the manufacturer’s instructions. Proper functioning of all laboratory equipment was assured through regular precision controls.

The laboratory reference ranges were as follows:

<table>
<thead>
<tr>
<th>Laboratory test</th>
<th>Reference range</th>
</tr>
</thead>
<tbody>
<tr>
<td>TSH</td>
<td>0.27 - 4.2 mIU/L</td>
</tr>
<tr>
<td>FT4</td>
<td>0.94 - 1.72 ng/dL</td>
</tr>
<tr>
<td>FT3</td>
<td>2.01 - 4.42 pg/mL</td>
</tr>
<tr>
<td>ALT</td>
<td>9-50 U/L</td>
</tr>
<tr>
<td>AST</td>
<td>15-40 U/L</td>
</tr>
<tr>
<td>ALP</td>
<td>38-126 U/L</td>
</tr>
<tr>
<td>GGT</td>
<td>12-43 U/L</td>
</tr>
</tbody>
</table>

**Operational definitions:** The diagnosis of **overt hypothyroidism** necessitated reduced serum free T4 < 0.94 ng/dl and elevated TSH levels > 4.20 μU/ml. Eu-thyroid state required normal TSH, FT4, and FT3 levels.

**Diabetes mellitus** was diagnosed according to American Diabetes Association, 2017. (16)

**Metabolic syndrome and dyslipidemia** were defined according to the final report of the Adult Treatment Panel III. (17)

**Abdominal Ultrasound Examination:** Abdominal ultrasound examinations were performed under standardized conditions by a qualified consultant sonographer using a real-
time electronic convex type scanner (Toshiba Nemio 20 with 3.75 MHz convex-type transducer). Examinations included assessment of the liver and spleen. The liver was assessed with respect to its size and the presence of hepatic steatosis. The list of parameters to be systematically evaluated included: right liver longitudinal span diameter, liver ultrasonographic echo-pattern, and diffuse hypo- or hyper-reflective echoes), portal vein diameter, splenic longitudinal span, and splenic vein diameter.

**Ultra-sound criteria for the diagnosis of NFLD:** Fatty liver (hepatic steatosis) diagnosis grounded on the criteria established by Charatcharoenwitthaya et al., \(^{(18)}\) and included: a hyper-echoic appearance of the liver parenchyma with fine, tightly packed echoes and posterior beam attenuation. Hepatomegaly was assessed according to liver diameters reported by Niederau et al. \(^{(19)}\) Measuring the longitudinal diameters by longitudinal scans in the mid-clavicular line and midline. Measurement results were interpreted as hepatomegally if right mid-clavicular longitudinal span of the liver >15.5 cm.

**The intervention:** Confering to the guideline for treatment of hypothyroidism subsidized by the American Thyroid Association and the American Association of Clinical Endocrinologists. \(^{(20)}\) Patients with overt hypothyroidism were prescribed LT4 supplementation to normalize TSH and FT4 (Euthyro, 25 μg and 50 μg per tablet, Merck Serono, Darmstadt, Germany). The initial dose was 50 μg/day. It was taken every day morning with water on empty stomach, 30 to 60 minutes before breakfast. \(^{(20)}\) Serum TSH and FT4 levels were re-evaluated six weeks later, and accordingly, the LT4 dose was adjusted until a state of euthyroidism (TSH of 0.3–3 mIU/L with a normal serum FT4 level) was achieved, and subsequently the dose of LT4 was maintained.

The average daily LT4 dose was 125 μg. All involved patients were re-evaluated every 12 weeks. Patient status was updated and recorded at each visit, including any recent medical problems, medications, surgeries, and recognizable alterations in lifestyle (e.g., intense exercise or vegetarian diet). Adherence to LT4 intake was monitored by direct question and counting any unused tablets every visit. All participants received follow-up for 6 months. There was no drop out of the follow up as all of the participants receive their healthcare exclusively at the University medical center.

**Study End Points:** In the present study, the primary endpoints was the effect of LT4 replacement therapy on the prevalence of NAFLD, the serum liver enzymes ALT, AST, GGT, and ALP, and ultrasound characteristics of the liver. The secondary endpoints were changes in BMI, WC, lipid profile including TC, TG, LDL-C, and HDL-C, and prevalence of metabolic syndrome before and after LT4 therapy.
Sample Size: A sample size of 322 was calculated using the statistical formula \[ n = \frac{Z^2pq}{d^2} \], \(^{(21)}\) where \( n \) = sample size, \( Z \) = confidence interval (CI), \( p \) = prevalence rate (in %), \( q = 1-p \), \( d \) = degree of precision. A confidence interval of 95\%, and degree of precision (margin of error) set at 5\% was used. Prevalence rate of 30\% for NAFLD was identified.\(^{(3,4)}\) The prevalence of hypothyroidism is not precisely known, however, a rate of 5\% was identified in developed countries.\(^{(22)}\) Nonetheless, a total of 650 subjects were included in the current study, divided into 325 subjects with overt hypothyroidism (case group), and 325 subjects without hypothyroidism (control group). The study was conducted in accordance with the principles of good clinical practice, and was approved by the medical ethics committee of Umm Al-Qura University. All participants provided written informed consent after explanation of the objectives of the study and being assured of keeping their information confidential.

Data management: Data collected through physical examination, laboratory investigations and ultrasonography were tabulated and analyzed statistically by the SPSS software program, Version 20. Quantitative variables were presented as mean and standard deviation (SDs), while qualitative variables were presented as numbers and percentages. To evaluate the variances on quantitative variables, unpaired t test was used, while qualitative variables were compared with Pearson’s chi-square test. To study the influence of LT4 replacement therapy on subjects with NAFLD in the hypothyroid group, a paired-samples t-test was used. A two-tailed value of \( p < 0.05 \) was considered significant.

Results:

A total of 650 participants were involved in this study. The mean age of participants was 45.22±5.04 years old, and 369 (56.8\%) were females. Participants were divided into 325 subjects with overt hypothyroidism (case group), and 325 subjects without hypothyroidism (control group). There was 136 (41.8\%) males in the case group, and 145 (44.6\%) males in the control group (\( p = 0.476 \)). Mean age of participants was 44.96± 5.277 in the case group, and 45.48±4.79 in the control group (\( p = 0.192 \)).

Table (1) compares the metabolic characteristics of both groups, where subjects in the case group had significantly higher mean values of WC (\( p = 0.005 \)), serum TC, TG, HDL-C, LDL-C, HbA1c, SBP and DBP (\( p < 0.001 \)), as well as significantly higher number and percentage of subjects with dyslipidemia (\( p = 0.001 \)), hypertension (\( p = < 0.001 \)), type 2 diabetes mellitus (\( p = 0.006 \)), and metabolic syndrome (\( p < 0.001 \)).

Table (2) compares the liver biochemical and ultrasound characteristics of both groups, where subjects in the case group revealed significantly higher mean values of the liver
transaminases; ALT, AST, GGT (p < 0.001), and alkaline phosphatase (p = 0.031). Liver ultrasound revealed significantly higher mean values of the right liver lobe span and portal vein diameter (p < 0.001). Overall prevalence of ultrasound diagnosed NAFLD in all participants was 229 (35.2%). The prevalence of NAFLD was significantly higher in the case group compared to their controls [146 (44.9) versus 83 (25.5), p < 0.001].

Table (3) reveals the effect of 12 months of LT4 replacement therapy on subjects with NAFLD in the case group, where there was significant reduction in the mean values of the metabolic variables [BMI, WC, TC, TG, LDL-C (p < 0.001), FBG (P =0.012), and HbA1c (p = 0.031)], and non-significant increase in HDL-C (p = 0.187). The number and percentage of subjects with dyslipidemia, and those with metabolic syndrome was significantly decreased (p < 0.001).

Moreover, as shown in table 4, the 12 months of LT4 replacement therapy was associated with significant reduction in the mean serum values of the liver enzymes ALT, AST, and GGT (p < 0.001), but not ALP (p = 0.073), while liver ultrasound showed significantly reduced mean values of the right liver lobe span, and portal vein diameter (p < 0.001). Apparently, the prevalence of ultrasound diagnosed NAFLD was significantly reduced (35.6%; p < 0.001).

Discussion: The association between hypothyroidism and NAFLD has been the focus of many researches beginning with that by Liangpunsakul and Chalasani in 2003. Few controversial results have been reported, whereas several studies have established the association between hypothyroidism and NAFLD, in concordance with the findings of the current study.

Most recently, Guo et al., in their large meta-analysis involving 26 observational studies, concluded that subjects with NAFLD exhibited significantly higher TSH levels compared to those without NAFLD, and that hypothyroidism was associated with a significantly higher risk of NAFLD.

In contrast, no significant association could be identified by Ittermann et al. and Ludwig et al. for TSH. Also, Jaruvongvanich et al., in their large meta-analysis, demonstrated that NAFLD was not associated with subclinical, overt, and unclassified hypothyroidism.

The close connection between hypothyroidism and metabolic syndrome is well established, and individuals with overt hypothyroidism often show features of the metabolic syndrome. Even more, a mutual link between both was documented (e.g., overweight/obesity) as a feature of metabolic syndrome, may mask the effects of thyroid hormones on the liver, by markedly disturbing glucose and lipid metabolism.

Moreover, as demonstrated in the current study, hypothyroidism was associated with increased levels of atherogenic dyslipidemia...
(LDL-C, TG) which serve to increase accumulation of fat inside the liver.\(^{32}\) Data has proposed that atherogenic cholesterols were related to NAFLD either. The mechanism underlying hyperlipidemia in hypothyroidism is reduced hepatic triglyceride lipase and increased fatty acid oxidation, \(^{33}\) producing increased hepatic inflow of triglycerides inside the liver and the development of NAFLD.

Moreover, a direct regulatory effect of TSH on liver lipid metabolism has been described. Hepatocytes had functional TSH receptor (TSHR) expression, and TSH binding to its receptors on hepatocytes up regulate hepatic cholesterol synthesis, and consequently upsurge cholesterol accumulation in the liver.\(^{34}\) Further, a role of TSH in regulating TG metabolism was described through stimulating TG buildup in hepatocytes brought by a fat-rich diet in mice. \(^{35}\)

The current study was grounded on overt hypothyroidism and revealed that normalizing the raised TSH, and the low T4 via appropriate LT4 supplement could significantly reduce the prevalence of NAFLD. The findings of this work are parallel to former studies that indicated the role of raised TSH in the progression of NAFLD.

Consistent with the present study, Liu et al., in their post-hoc randomized controlled trial involving 360 patients with significant subclinical hypothyroid, LT4 replacement for 15 months was associated with significant reduction in the serum liver enzyme, and 50% reduction in the prevalence of ultrasound diagnosed NAFLD (48.5% before LT4 replacement, versus 24.2% after LT4 replacement, \(p = 0.041\)).\(^{12}\) Impressively, Bruinstroop et al in their recent study on euthyroid subjects with type 2 diabetes and NAFLD, demonstrated that supplementation with low dose LT4 for as short as 4 months was accompanied with a substantial decrease of the intra-hepatic fat content, as measured by magnetic resonance spectroscopy. \(^{36}\)

In addition to the reduced prevalence of NAFLD on LT4 therapy, parallel to the findings of the current study, Chaker et al recognized that replacement therapy with LT4 to treat hypothyroidism was accompanied with a significant decrease in BMI and serum lipids. \(^{15}\) Several data have indicated that hypothyroidism is associated with higher prevalence of dyslipidemia compared with euthyroid subjects.\(^{32}\) Dyslipidemia is associated with a higher risk for NAFLD. \(^{33}\) In the current study, the prevalence of dyslipidemia was as high as 73.3% among hypothyroid patients who had been diagnosed with NAFLD, which is significantly higher compared with those without NAFLD.

The current study revealed that subjects with overt hypothyroid who received LT4 supplement demonstrated a significant decline in mean TC and TG. Data has proposed that atherogenic cholesterols were related to
NAFLD. Generally, this study suggests that the decreased serum TC and TG levels, via LT4 therapy, might relate to the improvement of NAFLD.

Another interesting outcome of the current study was that hypothyroid patients with NAFLD who received LT4 replacement presented a significant reduction in BMI. An independent consequence of obesity on liver fat is well recognized, and evidence has established that weight reduction is associated with a substantial improvement in the severity of NAFLD. It is likely that LT4 replacement could ease weight reduction by boosting the basal metabolic rate and consequently improving NAFLD.

Further studies are required to explore the exact mechanism underlies the advantages of LT4 replacement on NAFLD in hypothyroid patients.

Conclusions: This study demonstrated a significant association between overt hypothyroidism and the increased prevalence of NAFLD. Moreover, the current study revealed an advantageous effect of LT4 replacement on NAFLD in patients with overt hypothyroidism bringing out a significant decrease in the prevalence of NAFLD and serum liver enzymes. Therefore, based on these results, the importance of detection of NAFLD in patients with thyroid dysfunction is suggested, and treatment of overt hypothyroidism with proper LT4 supplementation may be an effective choice for improving NAFLD. Validation of the clinical values of LT4 supplementation on NAFLD with histological endpoints are needed through double-blind, placebo-controlled trials.

Fund: The research was conducted with no fund.

Conflict of Interest: There was no conflict of interest.

References:
5. Mehran L, Amouzegar A, Azizi F. Thyroid disease and the metabolic syndrome. Curr


There were significantly higher values of metabolic variables among subjects with overt hypothyroid (p < 0.05).
Table 2. Liver Biochemical and Ultrasound Characteristics of Subjects with Overt Hypothyroidism and their Controls

<table>
<thead>
<tr>
<th>Variable</th>
<th>Hypothyroidism (N=325)</th>
<th>Controls (N=325)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Liver enzymes:</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>▪ ALT (IU/L)</td>
<td>44.13±17.97</td>
<td>19.89±6.11</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>▪ AST (IU/L)</td>
<td>41.03±7.82</td>
<td>20.73±6.33</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>▪ GTT (IU/L)</td>
<td>43.85±16.58</td>
<td>35.59±20</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>▪ Alkaline phosphatase (IU/L)</td>
<td>71.66±14.02</td>
<td>68±12.64</td>
<td>0.031</td>
</tr>
<tr>
<td><strong>Liver ultrasound:</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>▪ Right liver lobe span (cm)</td>
<td>14.66±2.48</td>
<td>12.5±1.1</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>▪ Portal vein diameter (cm)</td>
<td>12.5±1.1</td>
<td>10.18±1.05</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>▪ Ultrasound-diagnosed NAFLD [N (%)]</td>
<td>146 (44.9)</td>
<td>83 (25.5)</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

There were significantly higher values of serum liver enzymes, and ultrasound liver measurements (p < 0.05), as well as significantly higher prevalence of NAFLD among subjects with overt hypothyroid compared to their controls [(146 (44.9) versus 83 (25.5); p < 0.001)].
Table (3): Metabolic Characteristics of Subjects with NAFLD in the Overt Hypothyroid Group, Before and After Levothyroxine Replacement Therapy

<table>
<thead>
<tr>
<th>Variable</th>
<th>NAFLD (N= 146)</th>
<th>Mean</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Before LT4 therapy</td>
<td>After LT4 therapy</td>
<td></td>
</tr>
<tr>
<td>▪ BMI</td>
<td>30.17±2.08</td>
<td>28.02±2.21</td>
<td>- 2.15±2.26</td>
</tr>
<tr>
<td>▪ WC (cm)</td>
<td>96.83±5.19</td>
<td>91.45±3.05</td>
<td>- 5.37±4.13</td>
</tr>
<tr>
<td>▪ TC (mg/dL)</td>
<td>236.63±20.68</td>
<td>218.39±17.4</td>
<td>-18.24±23.49</td>
</tr>
<tr>
<td>▪ TG (mg/dL)</td>
<td>190.75±40.04</td>
<td>142.89±28.66</td>
<td>- 47.86±45.75</td>
</tr>
<tr>
<td>▪ HDL-C (mg/dL)</td>
<td>42.22±5.67</td>
<td>43.04±6.12</td>
<td>+ 0.616±5.62</td>
</tr>
<tr>
<td>▪ LDL-C (mg/dL)</td>
<td>135.36±15.14</td>
<td>129.35±13.78</td>
<td>- 6.0±20.01</td>
</tr>
<tr>
<td>▪ Dyslipidemia [%]</td>
<td>107 (73.3)</td>
<td>78 (53.4)</td>
<td>-</td>
</tr>
<tr>
<td>▪ FBG (mg/dL)</td>
<td>124.64±17.77</td>
<td>119.41±17.68</td>
<td>- 5.22±</td>
</tr>
<tr>
<td>▪ HBA1C (%)</td>
<td>6.43±.76</td>
<td>6.3±0.527</td>
<td>- 0.135±0.75</td>
</tr>
<tr>
<td>▪ Metabolic syndrome [N (%)]*</td>
<td>98 (67.1)</td>
<td>69 (48.5)</td>
<td>-</td>
</tr>
</tbody>
</table>

*Chi square test.

There was significant statistical reduction in the values of metabolic variables (p < 0.05). There was no significant statistical difference as regard HDL-C (p = 0.187).
Table (4): Liver Biochemical and Ultrasound Characteristics of Subjects with NAFLD in the Overt Hypothyroid Group, Before and After Levothyroxine Replacement Therapy

<table>
<thead>
<tr>
<th>Variable</th>
<th>NAFLD (N= 146)</th>
<th>Mean</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Before LT4 therapy</td>
<td>After LT4 therapy</td>
<td></td>
</tr>
<tr>
<td>Liver enzymes:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>▪ ALT (IU/L)</td>
<td>49.66±17.87</td>
<td>38.47±3.98</td>
<td>11.19±17.54</td>
</tr>
<tr>
<td>▪ AST (IU/L)</td>
<td>42.29±7.69</td>
<td>34.47±13.13</td>
<td>7.815±11.86</td>
</tr>
<tr>
<td>▪ GTT (IU/L)</td>
<td>49.21±17.74</td>
<td>40.86±17.95</td>
<td>8.349±13.94</td>
</tr>
<tr>
<td>▪ ALP (IU/L)</td>
<td>75.68±13.58</td>
<td>73.47±10.85</td>
<td>2.21±14.99</td>
</tr>
<tr>
<td>Liver ultrasound:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>▪ Right liver lobe span (cm)</td>
<td>17.06±1.07</td>
<td>15.9±2.19</td>
<td>1.157±2.03</td>
</tr>
<tr>
<td>▪ Portal vein diameter (cm)</td>
<td>11.07±0.9</td>
<td>10.15±1.11</td>
<td>0.919±1.12</td>
</tr>
<tr>
<td>▪ Ultrasound diagnosed NAFLD [N (%)]*</td>
<td>146 (100)</td>
<td>94 (64.4)</td>
<td>-</td>
</tr>
</tbody>
</table>

Levothyroxine replacement therapy was associated with a significant reduction (35.6 %, p < 0.001) in the prevalence of NAFLD, and mean values of serum liver enzymes ALT, AST, and GGT, and ultrasound liver measurements (p < 0.001).
Coshorul al-ghadha al-drrqiya wa al-kbde dahnee ghir al-khohlwi: al-isla fil al'ahil al-ta'awubbiy bi-lafithiwrx bin

Mkhtat Mhfoos Shetla - Ahmd Slmnh Fisml

al-khlfiyah: al-sila biin Coshorul al-ghadha al-drrqiya wa al-kbde dahnee ghir al-khohlwi mjallal "Mtrdaa" lil-darasa miitlikatia biin al-drastas alal
Talibil al'ahil al-ta'awubbiy bi-lafithiwrx bin mfqetl. al-ahdafa: Chtef fiiddna al-drasa lil-darasa biin Coshorul al-ghadha al-drrqiya alunlni wa al-kbde dahnee ghir al-khohlwi. al-mnhjibj webt fhrbth: Shmtl
al-drasa 325 Mrbd Coshorul al-ghadha al-drrqiya alunlni hidhit titshixicq maqrnna biidhhd mttqabq miniby Mutbq fbiin al sni wa al-nugh
wa mmlkth kfltha jsm. wa Tmmr lmqrina b3nhill minn tinj al'ahwml meltalulmnyina wa anizmtn al-kbde wa mbsyrt mshxshinnin balakd dahnee ghir
al-khohlwi bullalwrtw mlwtdth. u tkrnt lmqrina lill mlshxshinnin balakd mshxshinin balakd dahnee ghir Coshorul al-ghadha al-drrqiya biidhh 12 shrnn.m

al'ahil al-ta'awubbiy bi-lafithiwrx bin. al-nrtkg: Mttswot umr mshxshinin biidd 5.04 biidd 45.22 (56.8) mtn lnln. u Atrht
al-nrtkg al mlshxshin biin mjwdaa 44.44% mdllll jz mghz dnn fbiin Mitdd mlshxshinin balakd dahnee
ghir al-khohlwi (44.44% mbqbl 25.5) w al'ahwml meltalulmnyina w mstwrttn anizmtn al-kbde mqrnnna lill mlshxshinin biin mjwdaa al-
w biidhh 12 shrnan" min al'ahil al-ta'awubbiy bi-lafithiwrx bin lill mlshxshinin biin mjwdaa Coshorul al-ghadha al-drrqiya alunlni dnu al-kbde dahnee ghir
al-khohlwi tnanqbst bbsyrt mshxshinin balakd dahnee ghir al-khohlwi bnsbta 35.6% w tnanqbst mstwrttn anizmtn al-kbde skll Mitdd wln
mgz. al-nlxlh: Tnhxl ss ddrasa uln jwdd Ulqll dtt Mzgh biin Coshorul al-ghadha al-drrqiya alunlni wa al-kbde dahnee ghir al-khohlwi. Kmma
Tnhxl ss Anl 12 shrran" min al'ahil al-ta'awubbiy bi-lafithiwrx bin mdl mlhwh lnsb mshxshinin balakd dahnee ghir al-khohlwi.